

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C.20231  
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 13 December 1999 (13.12.99)	Applicant's or agent's file reference IPD/P1203/WOD
International application No. PCT/GB99/01387	Priority date (day/month/year) 29 May 1998 (29.05.98)
International filing date (day/month/year) 05 May 1999 (05.05.99)	
Applicant BENNETT, Alice, Marie	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:  
23 November 1999 (23.11.99)

in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election  was  
 was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer Juan Cruz  Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference IPD/P1203/WOD	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB99/01387	International filing date (day/month/year) 05/05/1999	Priority date (day/month/year) 29/05/1998
International Patent Classification (IPC) or national classification and IPC C12N15/63		
Applicant THE SECRETARY OF STATE FOR DEFENCE et al.		RECEIVED OCT 26 2001 TECH CENTER 1600/2900

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 23/11/1999	Date of completion of this report 02.11.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx. 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Mennessier, T  Telephone No. +49 89 2399 8687



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/01387

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-13                   as originally filed

**Claims, No.:**

1-18                   as originally filed

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**Drawings, No.:**

1a,2-4               as originally filed

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2. The amendments have resulted in the cancellation of:

the description,      pages:  
 the claims,           Nos.:  
 the drawings,         sheets:

3.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application.  
 claims Nos. 16 and 17.

because:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB99/01387

the said international application, or the said claims Nos. 16 and 17 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos. .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)                  Yes: Claims 1-18  
                                  No: Claims

Inventive step (IS)           Yes: Claims 1-13 and 15-18 (partly)  
                                  No: Claims 14 and 15-18 (partly)

Industrial applicability (IA)   Yes: Claims 1-15 and 18  
                                  No: Claims

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**2. Citations and explanations**

**see separate sheet**

**VI. Certain documents cited**

**1. Certain published documents (Rule 70.10)**

and / or

**2. Non-written disclosures (Rule 70.9)**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
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**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/01387

**1. Comments with respect to item I**

Sequence listing pages 1-2 filed with the letter sent in reply to the invitation to furnish nucleotide sequence listing [Form ISA225] do not form part of the application (Rule 13<sup>ter</sup>.1(f) PCT).

**2. Comments with respect to item III**

Claims 16 and 17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**3. Comments with respect to item V**

**a) Documents cited**

Reference is made to the following documents:

- \* D1: *Viral Immunology*, 11(3), 1998, 109-117
- \* D2: *The Journal of General Virology*, 69, 1988, 3005-13
- \* D3: *Journal of Molecular Biology*, 210(4), 1989, 749-69

The inventor appears to have contributed to document D1 which can be regarded as a non-patent literature counterpart of the present application.

**b) Novelty (Article 33(2) PCT)**

The various aspects of the invention appear not to be disclosed in any of the documents belonging to the relevant state of the art, and, therefore can be acknowledged as new.

**c) Inventive step (Article 33(3) PCT)**

- (i) Furthermore, it is considered that none of the afore-mentioned

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/01387

documents would have suggested to a person skilled in the art at the priority date that the presence of a lysine residue at position 7 in the E2 protein of VEE would be capable of enhancing immunogenicity of a vaccine as defined in claim 1 compared to existing live attenuated vaccines such as the vaccine referred to as TC-83.

- (ii) Therefore, it can be acknowledged that the subject-matter of claims 1- 13 involves an inventive step, the same conclusion applying *de facto* to those embodiments of the inventions of claims 15-18 which are defined using a back-reference to any one of claims 1-13.
- (iii) From document D2 it can be derived that the 7.5K vaccinia promoter is appropriate to correctly express VEE genes inserted into a vaccinia virus. Furthermore, document D3 teaches that synthetic promoters efficient at increasing protein expression can be constructed which correspond to the 7.5K vaccinia promoter with mutations within the critical region AAAAgTaGAAAataTA. Therefore, it is considered that a person skilled in the art would have regarded it as obvious to combine the teachings of document D2 and D3 and would have been prompted to prepare a vaccinia virus vector encoding an attenuated form of the VEE virus capable of producing a protective immune response, the corresponding DNA sequence being placed under expression control of a such a synthetic 7.5K vaccinia promoter with a view to increasing the amount of VEE proteins produced.
- (iv) Consequently, it is considered that the subject-matter of the broadly formulated claim 14 does not involve an inventive step, the same conclusion applying *de facto* to those embodiments of the inventions of claims 15-18 which are defined using a back-reference to claim 14.

d) Industrial applicability (Article 33(4) PCT)

- (i) It is considered that the subject-matter of claims 1-15 and 18 is susceptible of industrial applicability.

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EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/01387

(ii) For the assessment of claims 16 and 17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. Comments with respect to item VI

Should the invention appear not to be entitled to the claimed priority date, document D1 should be taken into consideration when assessing whether the various aspects of the invention are new and involve an inventive step.

5. Comments with respect to item VIII

Claim 5 is objected to under Article 6 PCT for the following reasons:

(i) "BCG" is the abbreviation commonly used to designate the Bacillus Calmette-Guérin which is a not a virus but a bacterium; and

(ii) "BCC" would appear not to be an abbreviation commonly used in the field of virology. Therefore, it is not clear which virus is meant under the said abbreviation.



# The Patent Office

**Application No:** GB 9811433.3  
**Claims searched:** 1 to 15, 18

**Examiner:** Colin Sherrington  
**Date of search:** 4 August 1998

## Patents Act 1977 Search Report under Section 17

### Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.P): C3H(HB7M,HB7V)

Int Cl (Ed.6): A61K 39/12; C07K 14/18; C12N 15/86

Other: ONLINE: WPI, CLAIMS, DIALOG/BIOTECH

### Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims	
A	US 5185440 (NORTH CAROLINA STATE UNIVERSITY) - whole document	1, 15	PCT
A	US 5505947 (THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL) -whole document	1, 15	
A	J.gen.Virol. 1988,69,3005-3013 -Richard M.Kinney <i>et al.</i> "Recombinant Vaccinia/Venezuelan Equine Encephalitis (VEE) Virus Expresses VEE Structural Proteins"	14, 15	PCT
A	Virology 1995,206,994-1006 -Franziska B.Grieder <i>et al.</i> "Specific Restrictions in the Progression of Venezuelan Equine Encephalitis Virus-induced Disease Resulting from Single Amino Acid Changes in the Glycoproteins"	1, 15	

X Document indicating lack of novelty or inventive step	A Document indicating technological background and/or state of the art.
Y Document indicating lack of inventive step if combined with one or more other documents of same category.	P Document published on or after the declared priority date but before the filing date of this invention.
& Member of the same patent family	E Patent document published on or after, but with priority date earlier than, the filing date of this application.



## PATENT COOPERATION TREATY

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## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>IPD/P1203/WOD</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 99/ 01387</b>	International filing date ( <i>day/month/year</i> ) <b>05/05/1999</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>29/05/1998</b>
Applicant <b>THE SECRETARY OF STATE FOR DEFENCE et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

## 4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

**RECOMBINANT VENEZUELAN EQUINE ENCEPHALITIS VIRUS VACCINE**

## 5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

## 6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

 None of the figures.

## INTERNATIONAL SEARCH REPORT

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 16-17 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the vaccine.
2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/01387

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 6 C12N15/63 A61K39/12 A61K39/295

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 6 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KINNEY R M ET AL: "Recombinant vaccinia/Venezuelan equine encephalitis ( VEE ) virus expresses VEE structural proteins." JOURNAL OF GENERAL VIROLOGY, (1988 DEC) 69 ( PT 12) 3005-13. , XP002118353 cited in the application page 3005 -page 3006 page 3007; figure 1 ---	14-18
Y	DAVISON, ANDREW J. ET AL: "Structure of vaccinia virus early promoters" J. MOL. BIOL. (1989), 210(4), 749-69 , XP002118354 page 749 page 767, left-hand column -page 769, right-hand column ---	14-18

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

11 October 1999

Date of mailing of the international search report

22.10.99

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
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Authorized officer

Mennessier, T

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/01387

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KINNEY R M ET AL: "The full-length nucleotide sequences of the virulent Trinidad donkey strain of Venezuelan equine encephalitis virus and its attenuated vaccine derivative, strain TC-83." VIROLOGY, (1989 MAY) 170 (1) 19-30. , XP002117670 the whole document ---	1-18
A	HUNT A R ET AL: "Localization of a protective epitope on a Venezuelan equine encephalomyelitis ( VEE ) virus peptide that protects mice from both epizootic and enzootic VEE virus challenge and is immunogenic in horses." VACCINE, (1995 FEB) 13 (3) 281-8. , XP004057668 cited in the application the whole document ---	1-18
A	AGAPOV E V ET AL: "Localization of four antigenic sites involved in Venezuelan equine encephalomyelitis virus protection." ARCHIVES OF VIROLOGY, (1994) 139 (1-2) 173-81. , XP002117671 the whole document ---	1-18
A	US 5 185 440 A (JOHNSTON ROBERT E ET AL) 9 February 1993 (1993-02-09) the whole document ---	1-18
P,X	BENNETT A M ET AL: "Improved protection against Venezuelan equine encephalitis by genetic engineering of a recombinant vaccinia virus." VIRAL IMMUNOLOGY, (1998) 11 (3) 109-17. , XP002117672 the whole document -----	1-18

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/GB 99/01387

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5185440	A 09-02-1993	NONE	